the survival rate between the 2 latter groups was not statistically significant. 4 months after YAS injection, all surviving rats were given a 2nd i.p. injection of 10^6 YAS cells. All rats that had been treated with cyclophosphamide 2 days after the 1st YAS injection died, while 7 of 10 rats that had been given cyclophosphamide 5 days after the 1st YAS injection rejected tumor challenge and survived ($p < 0.001$). These 7 rats were resistant to further YAS challenges (data not shown).

Therefore, although the application of cyclophosphamide 2 or 5 days after YAS injection appeared to be equally effective against the tumor, resistance to a subsequent tumor challenge was demonstrable only in rats treated with the drug 5 days after YAS injection. The difference was probably due to the greater susceptibility of the immune system to cyclophosphamide during the early phase of the immune response to the tumor than later when the proliferation of the lymphoid cells subsided[2,3]. The data indicate that the timing of even a successful tumor chemotherapy may greatly influence the future resistance to the tumor in the cured animals.

Survival of rats treated with cyclophosphamide[a] after injection of Yoshida ascites sarcoma (YAS) cells[b], and resistance of the survived animals to the 2nd YAS inoculum

Cyclophosphamide given after the 1st YAS injection	No. of surviving/No. of treated rats After the 1st YAS injection[c]	After the 2nd YAS injection
No cyclophosphamide	0/21	-
2 days	14/21	0/10
5 days	10/21	7/10

[a] 120 mg/kg i.v.; [b] 10^6 cells/recipient i.p.; [c] Tumor-free survivors 4 months after tumor injection; [d] Challenged 4 months after the 1st YAS injection; tumor-free survivors 2 months after the challenge.

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Radioprotective effect of a protein free parathyroid extract

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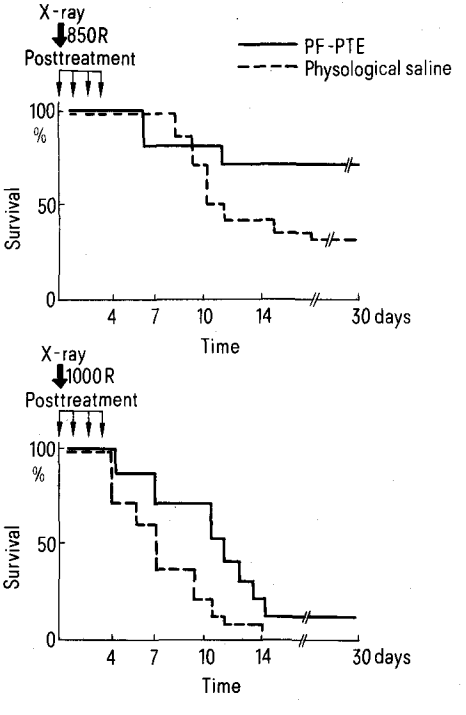
Summary. The radioprotective effect of a bovine protein-free parathyroid extract was studied in rats, being administered orally after irradiation. A significant increase in survival was found after treatment compared to controls. It is assumed that the extract contains a new, probably as yet unknown bioactive agent responsible for the radioprotection.

Rixon et al[1,2] have shown that the parathyroid extract (200 USP units parathormone, Eli Lilly and Co.) significantly prolonged the survival rate of whole body X-ray irradiated rats. They assumed that the radioprotective effect of the parathyroid extract was mainly due to the calcium mobilizing action of the parathormone, since the rise of calcium concentration in the mammalian tissues is known to reduce their radiosensitivity[3,4].

Present work is concerned with the protective efficacy of a protein-free and consequently calcium-inactive parathyroid extract (PF-PTE against 600 R, or 850 R, or 1000 R doses of X-ray irradiation. Preparation of PF-PTE was described previsouly[5]. The lyophylized PF-PTE was dissolved in physiological saline and administered perorally in 2 ml volume by a gastric tube to male CFE rats weighing 120–150 g. The whole body irradiations were delivered by a 'Super Liliput 200' X-ray apparatus 180 kV, 4 mA, 0,5 mm Cu filter, 50 cm from the target at a dose-rate of 7,8 R/min. Different groups of animals (n = 40 in each group) were irradiated with 600 R, or 850 R, or 1000 R. One other group was kept under the same conditions but without X-ray exposure. 20 of each group of the irradiated animals were treated with PF-PTE (0.1 mg/100 g of b.wt) firstly 3 h after the irradiation and on 3 successive days thereafter. The irradiated, but non-treated animals received physiological saline only. Survival in each group was observed and expressed as the number of rats still living 30 days after exposure (percent survival). The dose reduction factor (DRF) was also caclulated according van Bekkum[6]. All the nonirradiated, non-treated animals survived the 30th day. In the non-treated 600 R irradiated and the 600 R irradiated PF-PTE treated groups, all the animals were still alive on the 30th day.

The PF-PTE proved to be effective in increasing the 30 day survival of 850 R whole body irradiated animals (figure). The dose-reduction factor (DRF) at 850 R whole body irradiation is 1.35. The PF-PTE treatment was not effective



in prolonging the survival of 1000 R whole body irradiated animals. The DRF in this group was 1.05.

As Feuer et al.[5] pointed out, the deproteinized parathyroid extract lost its calcium mobilizing activity, but enhanced the vitamin A level in rats serum, proving the activity of the extract. Accordingly it can be excluded that the ratioprotective effect is the consequence of calcium mobilization from the bones or other Ca^{++} reservoirs. It seems reasonable to conclude that the PF-PTE contains some as yet unknown water-soluble bioactive agent responsible for the radioprotective effect. The elucidation of the chemical structure and properties of this bioactive agent including the synthesis will certainly permit a better understanding of the radioprotection of PF-PTE described in this paper.

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Effects of 6-hydroxydopamine on rat carotid body chief cells[1]

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Summary. Administration of 6-hydroxydopamine (6-OHDA) in concentrations high enough to cause degeneration of perivascular adrenergic nerve terminals has no morphological effect on the catecholamine-storing cells of the rat carotid body. Uptake of 6-OHDA by carotid body chief cells may be more selective than that exhibited by small-intensely-fluorescent cells and other catecholamine-storing cells which are affected by 6-OHDA. Alternatively, the sustentacular cells which envelope the chief cells may provide an effective barrier against the uptake of 6-OHDA.

The carotid body is one of several groups of arterial chemoreceptors which is sensitive to changes in blood pO_2, pCO_2 and pH. Although much is known concerning the cardiovascular and respiratory reflexes initiated by the arterial chemoreceptors, little is known about the identity of the actual receptor element or how this specialized organ functions as a chemoreceptor.

Recent investigations have suggested that the carotid body chief cells may function as interneurons, similar to the small-intensely-fluorescent (SIF) cells of the superior cervical ganglion[2]. Others suggest that the chief cells are sensory paraneurons which themselves represent the chemoreceptor element[3,4]. Additionally, a possible endocrine role for the chief cells has not been excluded[2,4]. Regardless of the function of the carotid body chief cells, most investigators agree that they contain one or more biogenic amines. Specifically, it has been demonstrated by fluorescence histochemistry[5], mass fragmentography[6], autoradiography[4,7], and biochemical analysis[8] that the carotid body chief cells contain dopamine, norepinephrine and serotonin. However, dopamine appears to be the predominant biogenic amine. Dopamine also has been demonstrated to be the primary biogenic amine of SIF cells[9].

The biogenic amines of the chief cells are stored within electron-dense cytoplasmic vesicles. The storage of biogenic amines in dense-cored vesicles is characteristic of a number of amine-containing cells including adrenergic nerve terminals, SIF cells, adrenal medullary cells, paraganglion cells and aortic body chief cells. Release of the carotid body chief cell biogenic amines appears to be intimately related to the function of these cells in chemoreception.

6-Hydroxydopamine (6-OHDA) has been shown to cause degeneration of the terminal portions of adrenergic and dopaminergic neurons as a result of its selective uptake and concentration in these terminals. Administration of 6-OHDA has resulted in similar morphological alterations in SIF cells of the paracervical ganglion[10] and adrenomedullary cells of young animals[11]. Hess[12] has demonstrated a decrease in catecholamine fluorescence of the carotid body following 6-OHDA treatment. However, Poullet-Krieger[13] has used 6-OHDA as an aid in identifying postganglionic sympathetic nerve terminals in the toad carotid labyrinth with no apparent effect on the amphibian's amine-containing labyrinth cells. The following study was initiated to investigate the ultrastructural effects of various dosages of 6-OHDA on the rat carotid body.

Materials and methods. Female Long-Evans rats weighing 200–250 g were administered single injections or 3 injections of 6-OHDA (100 mg/kg i.p.; Regis Chemical Co.) and sacrificed at the end of 1 week (single injection) or 48 h after the last injection (3 injections/week). All animals were anesthetized with Nembutal (50 mg/kg, i.p.) and perfused through the left ventricle with a solution of 3% glutaraldehyde, 1% paraformaldehyde in 0.1 M phosphate buffer at pH 7.2. The carotid bodies were post-fixed in 1% osmium tetroxide – 1.5% potassium ferrocyanide, en bloc stained in uranyl acetate, dehydrated in a graded series of ethanols, passed through propylene oxide and embedded in Epon-Araldite. Thin sections exhibiting light gold interference colors were stained with lead citrate and examined in a Siemens 1A electron microscope.

Another group of rats were given identical dosages of 6-OHDA and sacrificed for fluorescence histochemistry. Carotid bodies were frozen in liquid propane, freeze-dried, gased for 1 h in formaldehyde vapor generated from paraformaldehyde powder, and embedded in paraffin. 10 µm sections were mounted in Entellan-xylene and examined in a Leitz fluorescence microscope.

Results and discussion. Carotid body chief cells are characterized by an abundance of cytoplasmic vesicles which exhibit electron-dense cores and represent the storage sites for biogenic amines (figure 1). The perivascular nerve terminals within the carotid body exhibit several round mitochondria and an abundance of small dense-cored vesicles measuring approximately 40–50 nm in diameter (figure 2). Occasionally, a large dense-cored vesicle and several small electron-lucent vesicles also are observed within the terminals. However, the perivascular nerve terminals of rats which received a single or multiple injections